UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/853,880	05/14/2001	Gregory J. Riggins	00250.00003	6566

22907 7590 03/27/2003

BANNER & WITCOFF
1001 G STREET N W
SUITE 1100
WASHINGTON, DC 20001

EXAMINER
YAEN, CHRISTOPHER H

ART UNIT	PAPER NUMBER
1642	10

DATE MAILED: 03/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/853,880	Applicant(s) RIGGINS ET AL.	
	Examiner Christopher H Yaen	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *1-12,14 and 23-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13 and 15-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The examiner of the application has changed. This case has now been transferred as of 3/143/2003. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Christopher Yaen, Group Art Unit 1642.

Election/Restrictions

2. Applicant's election without traverse of group III in Paper No. 9 (filed 2/12/2003) is acknowledged. Applicant further elects GPNMB as the protein antigen.

3. Claims 1-12, 23-47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 9. Applicant is reminded to cancel all non-elected claims.

4. Claim 14 is withdrawn from further consideration as being drawn to a non-elected invention. Furthermore, claim 13 will be examined to the extent that it reads on an extracellular epitope of GPNMB only.

5. Therefore, claims 13, 15-22 are examined on the merits.

Information Disclosure Statement

6. The Information Disclosure Statement filed 5/14/2001 is acknowledged and considered. A signed copy of the IDS is attached hereto.

Claim Objections

7. Claim 13 is objected to because of the following informalities: the term "with" is missing from the line 3 between "glioblastoma" and "an". Appropriate correction is required.

Specification

8. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112, 2nd paragraph

9. Claims 13 and 15-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Regarding claim 13, 15, 17 and dependent claims thereof in the recitation of the term "GPNMB" it is a laboratory term of which could have multiple meanings and could be associate with multiple proteins. Because there is no associated sequence identification number, the metes and bounds of the term cannot be adequately defined.

11. Regarding claims 13 and dependent claims thereof in the recitation of the term "contacting", it is unclear as to what type of contacting is to take place. Does the applicant intend for the compound to be delivered by placing the antibody in a cell of a glioblastoma thereby "contacting" the antibody to the cells?

12. Regarding claims 13 and dependent claims thereof in the recitation of the phrase "extracellular epitope", it is indefinite because any combination of three or more amino

acids found within the extracellular domain of GPNMD is considered an epitope. As such the metes and bounds of the term cannot be adequately determined.

Claim Rejections - 35 USC § 112, 1st paragraph

13. Claims 13, and 15-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of screening by mining cells that overexpress the GPNMB gene, a method of PCR amplification, and western blotting of the GPNMB protein, does not reasonably provide enablement for a method of specifically delivering a reagent to a glioblastoma cell through the binding of an antibody specific for GPNMB conjugated to a reagent. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims of the instant invention are drawn to a method of directing an agent or reagent to a glioblastoma by contacting cells of a glioblastoma with an antibody directed against an epitope of GPNMB antigen conjugated to a reagent. The specification teaches the examination of several EST genes that show elevated levels in certain glioblastomas. The specification also teaches the hybridization of probes, the amplification of the GPNMB gene with primers, and a method of western blotting. However, nowhere in the specification does it specifically teach the delivery of an agent to a specific epitope on GPNMB, because the GPNMB protein has never actually been defined in the specification. There is little information of the protein itself. The specification does not teach whether the protein even actually exists. It is a well established fact that in normal circumstances, the level of transcription parallels that of

translation, however, in certain circumstances, the level of mRNA transcription is uncoupled from protein translation (Braun *et al* (Genes Dev 1989 Jun;3(6):793-802)). Therefore, given the fact that it is possible for some transcription and translation events to be unparalleled, it is possible GPNMB may not be translated from the unregulated mRNA detected in the instant invention. Even assuming that the protein is translated from the mRNA disclosed in the instant invention, how would one of skill in the art known whether there are even enough epitopes present on the surface of a glioblastoma for the method to be effective in delivering an agent. The method of the instant invention work based on the presence of an epitope found in GPNMB, if there is only a small percentage of protein found on the surface of the glioblastoma cell, then the antibody conjugate that is administered is left circulating in the blood stream thereby eliciting anti-idiotypic antibodies. Because the working examples of the instant invention have only provided a method of screening, amplification, hybridization, and other general methods of probing, it is not commensurate in scope to the claims that read on methods of delivering an reagent using an anybody to GPNMB because the specification has not provided the skilled artisan with enough information on the protein. Therefore, the skilled artisan is left to experiment to find out for themselves how to deliver a reagent to an epitope that may or may not be present on a glioblastoma.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 13, 15, 18-20, and 22 rejected under 35 U.S.C. 102(b) as being anticipated by Johnson *et al* (5,352,447). Claims of the instant invention are drawn to a method of delivering a reagent or agent to a glioblastoma with an antibody conjugated to the said reagent or agent, wherein the antibody is specific for an epitope of GPNMB. Johnson *et al* teach a method of treating metastatic lesions of tumors associated with the nervous system with an antibody that specifically recognizes transferrin receptor. Johnson *et al* further disclose of conjugating the said antibody to a toxin. Because the instant invention has not provided any specific SEQ ID No., the epitopes that are recognized by the transferrin receptor, in the absence of evidence to the contrary, are the same epitopes on the GPNMB protein. Therefore, the reagent coupled to the transferrin receptor will also be delivered to the GPNMB protein.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 13,15, and 18-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lazarus LH *et al* (J. Neurosci. Methods 1998 Mar;23(2):161-72) in view of either Reiter *et al* (Clin Cancer Res 1996 Feb;2(2):245-52) or Maynard *et al* (Annu. Rev Biomed Eng 2000;2:339-76). Claims are drawn to a method of delivering a reagent to a glioblastoma wherein the antibody specifically recognizes GPNMB, wherein the reagent is a chemotherapeutic agent, a cytotoxin, non-radioactive label, and a radioactive compound. Lazarus *et al* teach the assessment of 5 NMB (also known as GPNMB) antibodies and further contemplate the use of these antibodies for the localization techniques. Lazarus *et al* do not specifically teach the delivery of conjugated antibodies to GPNMB to glioblastomas. However, both Reiter *et al* and Maynard *et al* teach the conjugation of antibodies in general to either toxic agents or labels for the treatment or imaging of cancer.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of filing to delivery reagents to glioblastoma cells with an antibody that specifically recognizes GPNMB, wherein the antibody is conjugated with a toxin or label. One of ordinary skill in the art would have been motivated to do so because Lazarus *et al* taught five clones of antibodies that specifically recognized NMB, which is the same

as GPNMB, and further contemplated the use of the antibodies in localization. Both Reiter *et al* and Maynard *et al* taught techniques to conjugate antibodies with either toxins or labels and to use these antibody conjugates in the treatment, imaging or diagnosis of cancers. The skilled artisan would have been motivated to combine these references to arrive at the instantly claimed invention because the use of NMB antibodies would, in the absence of evidence to the contrary, specifically localize to any GPNMB antigen found on any type of cell. Furthermore, this localization when coupled with a antibody that is conjugated with a toxin or label would inherently deliver a reagent to a cell. Because GPNMB and NMB are the same protein and because the techniques of conjugating antibodies to toxins and labels were already available to the skilled artisan, this method is obvious over the prior art. Because the antibodies to GPNMB were already available and known to have high affinity for its ligand, and because method of conjugation are well established in the art, one of skill in the art would have expected a great deal of success in attempting this method.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-

308-4242 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
Art Unit 1642
March 24, 2003